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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,123	11/09/2005	Steffen Panzner	N015-7001US0	4731

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EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
12/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/556,123	PANZNER ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 19-44* is/are pending in the application.

4a) Of the above claim(s) *2,23-34 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-6, 19-22, 35 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/09 has been entered.

Amended claims 1-6, 19-43 and new claim 44 are pending in the present application.

Applicants elected previously with traverse of Group I, drawn to a depot system containing one or more protein or peptide active substances, a drug comprising the same depot system and **the first method** of using the same depot system by injecting the depot system subcutaneously or intramuscularly, in the reply filed on 2/20/2000. Applicant further elected the following species: (a) DPPC as a species of saturated synthetic phosphatidyl choline; (b) DC-Chol as a species of a cationic lipid; and (c) LHRH agonists as a species of protein and peptide active substances.

Claims 26-34 and 36 were withdrawn previously from further consideration because they are directed to non-elected inventions. Additionally, claims 2 and 23-25 were withdrawn previously from further consideration because they are directed to non-elected species.

Therefore, claims 1, 3-6, 19-22, 35 and 37-44 are examined on the merits herein with the above elected species.

Response to Amendment

The rejection under 35 U.S.C. 102(e) as being anticipated by either Gregoriadis et al. (US 7,008,791) or Unger et al. (US 5,770,222) was withdrawn in light of Applicant's amendment by the limitations "non-nucleic acid active substances" and "comprising the steps of Providing gas free liposomes……and combining with at least one cationic or pH sensitive cationic lipid".

The rejection under 35 U.S.C. 103(a) as being unpatentable over Unger et al. (US 5,770,222) in view of Gregoriadis et al. (US 7,008,791) was also withdrawn in light of Applicant's amendment.

Specification

The specification is objected because of the lack of antecedent for the terms "gas-free liposomes" and "non-nucleic acid active substances" being recited in the claims.

Claim Objections

Claims 1 and 44 are objected to because of the phrase "depot system, for burst release avoiding delayed release of active substances comprising gas-free liposomes having a membrane the liposomes consisting of" which is a run-on sentence without any proper punctuation mark (e.g., a comma). As written, it appears that the phrase refers to a depot system for burst release and avoiding delayed release of active substance.

Similarly, claim 38 is objected to because of the phrase "as depot system for burst release avoiding delayed release of non-nucleic acid active substances" which does not have a proper punctuation mark (e.g., a comma). As written, it appears that the phrase refers to a depot system for burst release and avoiding delayed release of active substance.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 19-22, 35 and 37-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended independent claims 1, 38 and new claim 44 recite the new negative limitation "**gas-free liposomes**". The claims are directed to a depot system comprising gas-free liposomes wherein the gas-free liposomes consist of the components recited in anyone of the independent claims 1, 38 and 44; and methods of using the same. **All liposome preparations containing active substances contain soluble or entrapped air molecules; and air composition is comprised of at least about 78% N_2; 20.95% O2; 0.93% Argon gases**. Unger et al (US 5,770,222) also indicated clearly that air

contains gases (see at least col. 5, lines 11-26). Additionally, amended claim 38 recite the limitation "**comprising the steps of Providing gas free liposomes having a size of between about 20-1000 nm….and combining with at least one cationic or pH sensitive cationic lipid**"; along with another negative limitation "**non-nucleic acid active substances**". The specification as originally filed does not provide a written support for the negative limitations of "gas-free liposomes" and "non-nucleic acid active substances", as well as a method for comprising the steps of combining gas free liposomes having a size of between about 20-1000 nm **with** at least one cationic or pH sensitive cationic lipid in the claims as now claimed. In the amendment filed on 9/24/09, Applicants failed to point out the specific page number and/or line number that provide support for these new limitations. It should also be noted that since the originally filed specification does not have a written support specifically for the preparation and use of any liposome composition free of soluble or entrapped air molecules which are composed of gas molecules or any other nucleic acids (e.g., gene, expression vectors, nucleic acids encoding a protein or a peptide) **apart from oligonucleotides (e.g., antisense oligonucleotides, small interfering RNA, decoy oligonucleotides, aptamers, spiegelmers, ribozymes) as active substances** (see pages 8-9 and example 8 of the instant specification), Applicants can not exclude these embodiments in the negative limitations "gas-free liposomes" and "non-nucleic acid active substances" as now recited by the instant claims. Please also note that M.P.E.P. provides that **if alternative embodiments are positively recited in the specification, they may be**

explicitly excluded from the claims (M.P.E.P. 2173.05(i), citing *In re Johnson* 558 F.2d 1008).

Therefore, given the lack of sufficient guidance provided by the originally filed specification, it would appear that Applicants did not contemplate and/or have possession of invention as now broadly claimed at the time the application was filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, 19-22, 35 and 37-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, independent claims 1 and 44 recite the broad recitation "depot system, for burst release avoiding delayed release of active substances **comprising gas-free liposomes**" and the claims also recite "**the liposomes consisting of**" which is the narrower statement of the range/limitation. Therefore, it is unclear **whether gas-free liposomes and/or any of the elements of the liposomes recited in either claim 1 or claim 44 is required or not required**. Clarification is requested because the metes and bounds of the claims are not clearly determined.

Claims 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a step of using liposomes because the recited steps of "providing gas-free liposomes" and "combining with at least one cationic or pH sensitive cationic lipid" are steps for preparing liposomes as depot system; and these recited steps are not using steps. Therefore, there is no nexus between the steps recited in the body of independent claim 38 with the preamble of the claim which recites specifically "A method of using liposomes as depot system". Additionally, there is no nexus between gas free liposomes comprising at least one active substance recited in the body of independent claim 38 with the preamble of the claim which recites specifically "using liposomes as depot system for the burst release avoiding delayed release of non-nucleic acid active substances".

Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is the subject for the recited step of injecting the depot system subcutaneously or intramuscularly.

Claim 44 provides for the use of "a depot system", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 44 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure and amended claims to be submitted by Applicants.

1. Fahl et al (US 7,045,550) teach at least **phospholipid based vesicles or liposomes having the following lipid components DSPC:Cholesterol:DOTAP in a 1:0.5:0.1 molar ratio for topical or local delivery of polyamine effectors to epithelial or mucosal cells to protect normal cells of cancer patients during cancer chemotherapy or radiotherapy** (see at least Summary of the Invention;

example 4 and issued claims). Fahl et al stated specifically "While this example is not intended to exclude the use of the other liposomal delivery systems, the nonionic liposome formulation was found to be a particularly efficient delivery when compared to other delivery systems" (col. 34, lines 6-9). The same teachings are also disclosed in WO 03/013245 (IDS).

2. Kedar et al (US 5,919480) teach a liposomal vaccine composition comprising a suspension of liposomes, which encapsulate an influenza subunit antigen and at least one immunostimulating cytokine for intraperitoneal, subcutaneous or intramuscular administration; **and the liposomes are formed from lipids such as DMPC, DMPG, cholesterol, DMTAP and combinations thereof** (see at least Summary of the Invention; col. 5, lines 40-52).

3. Male-Brune, R (US 5,660,855) teach a lipid composition comprising an aminomannose derivatized cholesterol with various lipids that include DOTAP, DSPC, DMPC, for the delivery of an imaging or therapeutic agent into the cytoplasm of a cell (see at least Summary of the Invention; col. 7, line 12 continues to line 34 of col. 8).

4. Pilkiewicz, F (WO 00/27359; IDS) disclose at least a composition having lipids and a bioactive agent (e.g., proteins, peptides, ribo-and deoxyribonucleic acids), **wherein the lipids (sixth lipid mixture) contain phosphatidylcholines (e.g., DPPC, DMPC, DSPC):positively-charged lipids (e.g., DOTAP):sterol compounds (cholesterol or esters of cholesterol) in the molar ratio of 1-20:0.5-20:0.5-5** (see at least Summary of the Invention and pages 5-6).

5. Boulikas, T (US 2003/0072794) teach that leuprolide among many other antineoplastic drugs can be encapsulated in a liposomal composition suitable for subcutaneously, intramuscularly and intratumorally injection (see paragraphs 52-74).

Conclusions

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN/
Primary Examiner, Art Unit 1633